

Artificial Intelligence and Mechanical Circulatory Support



Song Li, MD^a, Gavin W. Hickey, MD^b, Matthew M. Lander, MD^c,
Manreet K. Kanwar, MD^{c,*}

KEYWORDS

• Artificial intelligence • Machine learning • Mechanical circulatory support • Heart failure

KEY POINTS

- Artificial intelligence/machine learning has shown promising results in identifying patients appropriate for mechanical circulatory support therapy, predicting risks after mechanical circulatory support device implantation, and monitoring for adverse events.
- State-of-the-art machine learning algorithms, leveraging new data sources, stand to further expand artificial intelligence capabilities in mechanical circulatory support.
- Clinical implementation of artificial intelligence in mechanical circulatory support has been very limited.
- An interdisciplinary workforce is needed to demonstrate artificial intelligence's clinical efficacy, reliability, transparency, and equity to drive implementation.

HISTORY

Alan Turing initially explored the mathematical possibility of artificial intelligence (AI) in his 1950 paper, *Computing Machinery and Intelligence*, in which he conceptually discussed how to build intelligent machines¹. In 1956, the logic theorist was designed as a program to mimic the problem-solving skills of a human and presented at the Dartmouth Summer Research Project on AI. This work catalyzed the next 2 decades of AI research, which was marked by multiple success stories and setbacks. One of the biggest setbacks was the lack of computational power for the substantial needs of AI, at the time. In the 1980s, AI was reignited by an expansion of algorithmic tools—deep learning techniques, which allowed computers to learn using experience and mimic the decision-making process of a human expert.

However, it was only in the 1990s and 2000s that several landmark goals of AI were achieved. These included spoken language interpretation and an increase in computer storage limits, as well as processing speeds. This has heralded the age of “big data”—an age where we have the capacity to collect huge sums of information and apply AI to advance the fields of technology, banking, marketing, and entertainment, as well as medicine.

In recent years, there has been a significant increase in medical research using applications of various aspects of AI, especially in cardiovascular medicine. Physicians have long needed to identify, quantify, correlate, and process complex relationships among various data and patient outcomes. There is increasing demand to provide faster, more personalized care, lower costs, and decrease hospital readmissions and mortality by using sophisticated algorithms that can process

^a Division of Cardiology, University of Washington, 1959 Northeast Pacific Street, Seattle, WA 98195, USA;

^b Division of Cardiology, University of Pittsburgh School of Medicine, 200 Lothrop Street, PUH, 5B, Pittsburgh, PA 15213, USA; ^c Cardiovascular Institute, Allegheny Health Network, 320 E North Avenue, Pittsburgh, PA 15212, USA

* Corresponding author.

E-mail address: Manreet.KANWAR@ahn.org

Twitter: [@lisong2003](https://twitter.com/lisong2003) (S.L.); [@GavHick](https://twitter.com/GavHick) (G.W.H.); [@MattLanderMD](https://twitter.com/MattLanderMD) (M.M.L.); [@manreetkanwar](https://twitter.com/manreetkanwar) (M.K.K.)

VISIT...

LANZAROTE
Caliente.COM

patterns from large datasets. AI has the potential to exploit increasingly available large datasets in advancing patient care. It is hoped that AI will simplify the practices and processes of health care by performing tasks that are typically done by humans, but in less time and more economically. Initially dismissed by many as purely theoretical, with little potential on clinical workflow or patient care, AI in health care is projected to reach a \$150 billion valuation in the next 5 years.²

RELEVANCE

People who suffer from end-stage heart failure (HF) face debilitating symptoms, frequent hospitalizations, and high medical costs.^{3–5} Mechanical circulatory support (MCS) such as durable left ventricular assist device (LVAD) is a therapy proven to improve quality of life and mortality in patients with end-stage HF.^{6–8} From early recognition of disease progression, to establishment of LVAD candidacy to the postoperative period, there are numerous areas where complex decision-making is necessary. AI is uniquely suited for application in this field.

Estimates are that those implanted with durable LVADs are only a fraction of those potentially eligible. There is an under-recognition of these patients as they suffer through the vicious cycle of end-stage HF. This situation may be expected when advanced HF expertise is concentrated at large referral centers while many potential LVAD candidates present and re-present at smaller community hospitals. Although there is a dearth of advanced HF-trained cardiologists to have a meaningful impact on timely recognition and referral of patients with end-stage HF, AI can help. Systems can be created whereby AI allows automatic detection of cardiogenic shock or “frequent flyer” readmissions and recommends referral to a tertiary care center. Similarly, community hospitals may not have the training to provide appropriate care to a patient on MCS who arrives emergently, something with which AI can also assist.

Although recent LVAD technology advances have improved outcomes, adverse event rates remain unacceptably high.⁹ This factor places an emphasis on the appropriate timing of therapy to maximize benefit and minimize harm to the patient. Assessment of the LVAD candidate is important both to support the patient’s acceptance and understanding but also to prognosticate their perioperative risk. Another important element of candidacy is the preoperative assessment of the patient’s right ventricle (RV). Current risk scores and diagnostic tools have proven limited in

accurately predicting postoperative right ventricular failure.^{10–13} There are often innumerable data points to select from, including echocardiography, cardiac catheterization, and laboratory studies. The relationships and associations these data may or may not have with outcomes lends itself to the use of AI as a powerful tool to provide clarity in RV failure prediction.

An electronic device such as an LVAD that generates extensive data every minute is a distinctive opportunity for AI to understand, predict, and hopefully decrease adverse events. This constant stream of information is ripe to be transformed into actionable algorithms for both the patient and LVAD team. Full automation—an integrated LVAD AI system—has the potential to revolutionize quality of life and clinical outcomes, as it manages alarming trends on the go and intercedes before harm is incurred.

MACHINE LEARNING TECHNIQUES

AI is a term that broadly describes methods that allow computers to complete functions typically done by humans.¹⁴ Machine learning (ML) describes numerous computerized techniques that generate a predictive model from an algorithm and data. The typical workflow for an ML algorithm is data input followed by model training and testing, and finally the output comprising the predictions made.¹⁵ An ML model needs to be “properly learned” to be effective, meaning that predictions are accurate with both training and testing data. If a trained ML model loses accuracy on new data, it is said to be overfit.¹⁶ Conversely, a model that does not accurately predict training data is underfit, usually occurring when a model is too simplistic. Data quality can also affect model performance; excessive, heterogeneous, or missing data points can all negatively impact output accuracy.

Supervised and unsupervised learning are the 2 main categories of ML.¹⁵ Supervised learning is done when the sample is labeled, for example, when the desired output is known in the training data. Unsupervised methods are applied if the data are unlabeled. Patterns are, therefore, derived from the input data to create groups, such as in hierarchical clustering or principal components analysis. By identifying similar groups in the input data, new relationships and connections can be made. The output of unsupervised ML can even be entered into a supervised approach, which takes the new input and can train a model to make accurate predictions. A semisupervised approach can infer labels from a small amount of labeled data for a large amount of unlabeled data, allowing for better performance and lower costs. Ensemble

learning allows for the combination of multiple models that may identify different patterns into one more robust prediction algorithm.

As computing technology improves, so do the capabilities of ML. Deep learning describes methods that use neural network layers to achieve the desired output. The most basic neural network has 3 layers: an input layer, a hidden layer, and an output layer. However, a deep neural network can have multiple hidden layers that can sequentially analyze and transform the input data into unique patterns not achievable by other techniques. More complicated networks allow for the algorithm to learn and minimize error via a process called back propagation.¹⁷ Training such a system generally requires very large datasets, owing to the numerous hidden layers. There is also a black box–like effect with these methods as interpreting the prediction is challenged by the complex and hidden process that creates the output.

Today, there are many innovative applications of ML to the field of medicine. Computer vision has recently evolved exponentially as computing power has improved and ML has matured. It encompasses the use of ML (often neural networks) to allow for the perception of visual stimuli, which may translate into detection, classification, or localization.¹⁸ The obvious applications are to radiology, pathology, and so on, to detect patterns that may otherwise be missed by even the most experienced clinicians, improving diagnostic performance.^{19–21} Strokes can be found, cancers screened for, and even COVID-19 detection models have been developed.^{22–24} In cardiology specifically, computer vision can be trained to classify pulmonary hypertension, cardiac amyloid, and hypertrophic cardiomyopathy from echocardiographic images.^{25,26}

As discussed elsewhere in this article, ML algorithms require very large datasets when multilayered and complex networks are created. Changing the distribution of a model often necessitates the creation of another large training dataset, which can be logistically challenging and expensive. Transfer learning allows for the retention of the knowledge extracted from a previously trained algorithm to be conveyed to a new model without having to go through retraining from scratch. For example, a neural network already trained for classification of chest radiographs may be able to be successfully applied to COVID-19 pneumonia recognition via transfer learning.²⁷ These techniques can leverage complex ML networks trained on large datasets and apply them to similar but different domains and yet maintain performance.

Bidirectional encoder representations from transformers is a newer model developed by researchers at Google AI Language.²⁸ It is a major

step forward in ML as it applies to natural language processing (NLP). By reading a sequence of words in a nondirectional manner with attention mechanism, the model can learn the context of a word from what surrounds it. Through a process called fine tuning, the model can be trained to achieve predictive performance never previously attained. The applications are myriad; bidirectional encoder representations from transformers techniques can be used to deploy powerful data extraction to electronic health records (EHR), enabling highly accurate chart review efforts.²⁹

CLINICAL APPLICATIONS

In recent years, with the exponential growth of AI research in medicine, there has been a wide range of AI/ML applications in various MCS-related fields (Fig. 1). In this review, we attempt to delineate the applications of AI/ML in MCS from 2 different angles. One angle categorizes the various AI/ML applications by their intended clinical purposes. In the literature thus far, AI/ML has been used to risk stratify patients with HF to identify high-risk patients appropriate for MCS therapy, predict outcomes after MCS device implantation, and monitor MCS patients for adverse events. The other angle analyzes current AI/ML applications from a technical aspect, focusing on innovations in ML algorithms and model performance compared with traditional statistics. From this angle, AI/ML applications in MCS have used a variety of cutting-edge tree-based, Bayesian, and neural network models. It is also important to note 2 ML specializations that are unique to medicine and to MCS: medical audio/image analysis and EHR analysis.

Clinical Perspective

Beginning with the clinical perspective, the first area AI/ML can aid MCS therapy is to better identify high-risk patients with HF to be evaluated for MCS therapy. The optimal timing of advanced HF therapy referral for ambulatory outpatients is still unclear and, despite available clinical support tools, many patients are still referred too late. Many patients, especially in rural areas, may also lack access to health care providers familiar with MCS therapy. Although patients with acute cardiogenic shock are more readily identifiable, the decision to and the timing of transfer to a hospital with a higher level of available MCS therapy are also not well-known.

In this area, some recent research studies are laying the foundation for AI/ML to play an active role in the future. In 2017, Choi and colleagues³⁰ applied a neural network to a large EHR database to predict the incidence of HF 12 to 18 months in

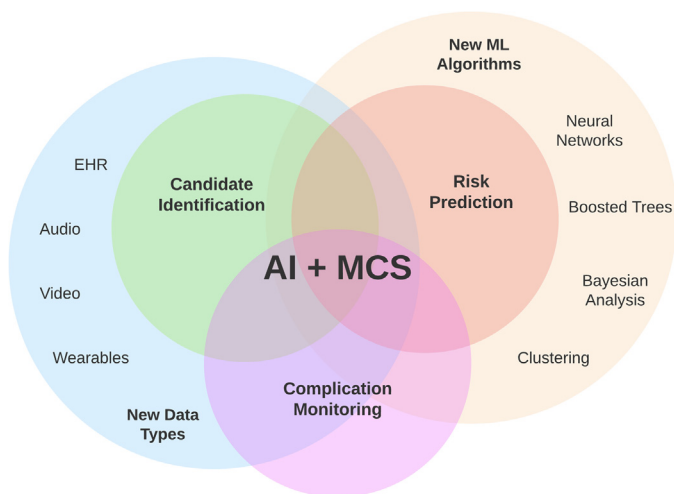


Fig. 1. Areas of applications of AI/ML in MCS. EHR, electronic health record.

the future and achieved an area under the curve (AUC) of 0.883, which represented a significant improvement from logistic regression. Later studies applied ML algorithm to predict mortality risk in large HF cohorts. Adler and colleagues³¹ applied a boosted decision tree algorithm (Ada-Boost) to a cohort of patients with HF identified by querying the EHR and achieved higher accuracy (AUC, 0.88) than 3 traditional risk models (AUC, 0.63–0.78) in predicting mortality risk. Greenberg and colleagues³² tested the same ML model across the spectrum of left ventricular ejection fraction and found similarly good risk discrimination in patients with HF with a reduced, midrange, or preserved left ventricular ejection fraction (AUC, 0.83–0.89). Similarly, Jing and colleagues³³ applied a boosted tree-based model (XGBoost) to a large EHR database with 26,971 patients with HF and 276,819 clinical episodes and achieved an AUC of 0.77 for 1-year all-cause mortality. However, in this study the best ML model only slightly outperformed linear logistic regression (AUC, 0.74). In addition to stratifying mortality risk in patients with HF to identify high-risk patients for MCS therapy and/or heart transplantation, it is also possible to train an ML model to predict the need for AHFT directly. Among patients with advanced HF in the Registry Evaluation of Vital Information for VADs in Ambulatory Life (REVIVAL) registry, Yao and colleagues³⁴ combined fuzzy set theory and neural network to predict the need for MCS or urgent heart transplant listing, and achieved excellent, yet only slightly better, model discrimination than logistic regression (AUC, 0.838 vs AUC, 0.812). ML has also been shown to achieve excellent mortality risk discrimination in the setting of acute HF.³⁵

The second area where AI/ML has been frequently applied is predicting risk after implantation of MCS devices. Knowing the likelihood of adverse events after MCS implantation allows clinicians to select patients most likely to benefit from MCS therapy and to potentially adopt strategies to decrease the risk of predicted adverse events. The research group of Antaki and colleagues has been playing a leading role in this area, using data from the Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) to predict adverse events after durable LVAD implantation.^{36–39} Their Bayesian models were able to predict 12-month mortality with an AUC of 0.70 and right ventricular failure with AUCs between 0.83 and 0.90 for different time points.^{36,37} A unique advantage of Bayesian models compared with other ML models is that Bayesian models are inherently explainable, both on a global (model) level and on a local (individual prediction) level. The ability to explain the inner workings of an ML model, compared with operating within a black box, is key to implementation of AI/ML in medicine, and will be discussed in more detail later. Other decision tree-based ML algorithms have also been tested to predict mortality after LVAD implantation with similarly good results.^{40,41} ML approaches allow for an improved visualization and understanding of adverse events burden after LVAD implantation.⁴² Two unique innovations in this area include an ML clustering analysis to identify sequential patterns of adverse events in patients with an LVAD³⁹ and a neural network model directly trained on echocardiogram videos to predict RV failure after LVAD implantation, which outperformed 2 traditional clinical risk models (AUC, 0.729 vs ACU, 0.605–0.616).⁴³

A third area in MCS where AI/ML has been applied is the monitoring of adverse events in patients after MCS device implantation. In this area, the first published application dates back to 1995 when Stöcklmayer and colleagues⁴⁴ applied a neural network model to a rotary blood pump in vitro to estimate left atrial pressure and identify suction and near-suction states. More recently, researchers have demonstrated the ability to use LVAD waveforms to predict impending pump failure in the HeartMate XVE LVAD and to identify cardiac arrhythmias in the DeBakey LVAD.^{45,46} Real-life out-of-hospital telemonitoring of patients with an LVAD has also been attempted in a cohort of 11 patients implanted with the HeartAssist 5 and acute VAD LVADs, which offer telemetric monitoring capabilities.⁴⁷ A total of 6216 alarm messages, mostly low-flow alarms owing to hypovolemia and suspected pump thrombosis, were received over a total of 2438 patient-days of follow-up. Manually reviewing all the alarms would certainly overwhelm the human resources of a typical VAD clinic; thus, AI is urgently needed to better identify high-risk alarm conditions needing urgent human attention. Telemonitoring using a wearable sensor has also been tested in ambulatory patients with HF to predict HF hospitalization. The LINK-HF study used a custom multisensor patch that collects continuous electrocardiograph waveform, 3-axis accelerometry, skin impedance, skin temperature, and information on activity and posture, and applied an ML similarity-based modeling to establish individualized physiologic baselines and detect deviations from the baseline.⁴⁸ The physiologic deviations were able to predict HF hospitalizations with 76% to 88% sensitivity and 85% specificity at a median of 6.5 days before hospitalization. It would be very interesting to see if a similar multisensor patch or, better yet, built-in sensors in future LVADs, can enable early detection of clinical decompensation.

Technical Perspective

From an ML technical perspective, AI/ML applications in MCS can be categorized into 2 main areas. One branch of research has strived to achieve better risk prediction by applying new ML algorithms and models to traditional datasets. The underlying logic is that traditional statistical models, such as frequently used linear and logistic regression models, are inadequate because they, in their basic forms, do not capture nonlinear relationships and variable interactions well. It is posited that MCS-related problems often have these complex relationships that are better modeled by more flexible ML algorithms such as decision-tree-based models (random forest, boosted trees), Bayesian

models, and neural networks. Many of the examples discussed elsewhere in this article fall into this category.^{31–33,36–38,40,41,49} Unsupervised ML is another example of applying new algorithms to existing datasets to gain new insights. In this regard, unsupervised clustering algorithms have been applied to traditional registry datasets to identify sequential patterns of adverse events in patients with an LVAD and to identify phenotypes of patients with cardiogenic shock, many of whom received temporary MCS devices.^{39,50}

Another branch of research applies ML algorithms to new data sources that are difficult to incorporate into traditional statistical models. EHR and audiovisual data are 2 prime examples. Non-ML research has leveraged EHRs by automatically querying tabular data from the EHR instead of manual data collection. However, truly incorporating the multimodal and longitudinal features of the EHR has only been feasible with recent advances in NLP and artificial neural networks. For example, Choi and colleagues³⁰ used recurrent neural networks on longitudinal EHR data to predict incident HF. Zhang and colleagues⁵¹ used NLP methods to identify New York Heart Association functional class from unstructured clinical notes in the EHR. Recent advances in transformer deep learning model using attention mechanism have been adopted for the EHR and is a promising tool for MCS applications.⁵²

Applications of AI/ML, especially deep neural networks, for audiovisual data also have great potential for MCS, because as the field is heavily dependent on acoustic and videographic information for decision-making. Electrocardiographs, echocardiograms, LVAD waveforms, LVAD sounds, and LVAD driveline exit site appearance are all potential data sources for AI/ML applications. Echocardiogram videos have been used directly to assess RV function, predict RV failure after LVAD implantation, and LVAD sound has been used to identify significant aortic regurgitation with good accuracy (AUC, 0.73).^{43,53–56} A group of innovative researchers applied convolutional neural network models to LVAD driveline photographs to identify driveline wound infections with an accuracy similar to human experts.⁵⁷ These types of AI/ML applications would allow patients to monitor the status of their LVADs closely from the convenience of their homes and have the potential to significantly decrease mortality and morbidity in patients with MCS devices.

LIMITATIONS AND ONGOING ADVANCEMENT

A combination of availability of large datasets and rapid technological advances in computing power

has led to the increased uptake and use of ML in multiple aspects of health care. However, there are some important limitations of AI for medical applications in general and in the field of MCS.

ML is data hungry, generally requiring much larger datasets than traditional statistics. An incredible amount of health data is now being generated, estimated at 10^{18} bytes from 2019 in the United States alone and growing at 48% annually.⁵⁸ Yet, the creation of large medical datasets still often relies on manual extraction of variables from the EHR and data labeling by human experts. Time-consuming and inherently biased by variable selection, this process is being vastly improved by recent advances. New interoperable EHR data structure such as fast health care interoperability resources and improvement in NLP now allow tens of thousands of data points be extracted for each patient with little human intervention. Using these methods on an EHR database of 216,221 patients, a research team from Google was able to extract more than 48 billion data points for ML modeling.⁵⁹ Having access to all available data points may allow ML algorithms to discover previously unknown but clinically relevant variables. However, this process can be computationally expensive, and the resultant models may be too slow for point-of-care use.

In addition to traditional EHRs, cloud-based platforms have been created. One such example of a large cloud based data marketplace is the American Heart Association Precision Medicine Platform.⁶⁰ In partnership with Amazon Web Services, the goal in its creation is to enhance and investigate the area of precision medicine via ML and big data. This and other large registries will be instrumental in allowing broader application of ML in health care.

Another significant limitation for AI use in MCS is the limited number of patients implanted. Data from the STS-INTERMACS annual report include 25,551 patients implanted with a continuous flow LVAD from 2010 to 2019.⁶¹ Although the STS-INTERMACS registry has a relatively large number of patients, the registry lacks granularity and is relatively heterogeneous, with data from 3 different types of continuous flow LVADs and at least 2 different surgical approaches (sternotomy and thoracotomy). Of the 25,551 LVADs implanted, only 15% (3901) were of the most contemporary LVAD still being implanted. Newer ML techniques such as transfer learning may prove immensely helpful to improve model performance when the sample size is small.

Despite advances in AI/ML, there are many examples of ML algorithms not performing better than traditional models. In an analysis on prediction of HF outcomes there was minimal

improvement in ML over traditional logistic regression models.⁶² A recent systematic review of ML compared with logistic regression for binary outcomes showed no benefit for ML over logistic regression.⁶³ Whether the sometimes mediocre performance of ML is due to the inherent noise and bias in the underlying datasets or can be improved with better ML algorithms remains to be seen.

Another limitation to the clinical use and acceptance of ML is the lack of transparency, the black box component of ML. Some of this reluctance can be attributed to a lack of understanding of ML and AI in general among the health care community, which can lead to mistrust of ML models and therefore a lack of use. In 1 instance, an early warning system for septic shock was developed using an ML algorithm. Despite excellent predictive accuracy, nurses and physicians did not find it useful clinically. Specifically, clinicians tended to trust their intuition over seemingly complex predictive algorithms.⁶⁴ One solution for the lack of transparency and interpretability is the use of explainable ML methods. For example, Shapley additive explanations (SHAP) is a unified framework that allows for more interpretable ML models.⁶⁵ SHAP values provide the estimated impact of each variable in the model as well as whether the effect is positive or negative. The use of SHAP provided valuable insights into the importance of each variable in a recent paper using ML to predict acute kidney injury after cardiac surgery.⁶⁶ The further development and use of explainable ML methods such as SHAP will likely improve the acceptance of ML models in clinical settings by both clinicians and patients.

INCORPORATION INTO CLINICAL PRACTICE

In the last 2 decades, there has been an explosion of AI applications in nearly all industries and all facets of life. The adoption of AI in medicine has tremendous promise in fulfilling the quadruple aims of modern health care systems, namely, improving the experience of care, improving the health of populations, decreasing per capita costs, and improving the work-life of health care providers.⁶⁷ However, even though AI/ML research in medicine has accelerated to more than 16,000 publications in 2020 in the MEDLINE database, the implementation of AI in routine clinical use has been scantily reported.⁶⁸ Health care professionals are key stakeholders to evaluate barriers and define strategies to drive AI implementation in medicine. To achieve this goal, an interdisciplinary workforce is needed to integrate the expertise of health care providers, AI/ML developers, health system

leaders, ethicists, and patients. A cross-disciplinary curriculum must be developed and deployed so that health care providers can assess and correctly use AI products and services akin to other medical products. Vice versa, such curriculum can empower AI/ML developers to build AI products that adhere to the safety, efficacy, and ethical principles of health care. Having a shared knowledge base and language is critical to effective collaboration in such interdisciplinary health AI teams.

In addition to an interdisciplinary health AI workforce, another key barrier to implementing health AI products is ensuring the quality of the AI products. Health AI products are different from traditional medical treatments or devices where safety and efficacy are the 2 primary considerations. Although the standards of testing for health AI products are still being hotly debated among developers, users, investors, and regulators, it is clear that health AI products require testing in new domains. However, first and foremost, similar to other medical products, health AI products need to show improvement not only in statistical accuracy, but also in clinical outcomes. A second and related domain is reliability, which means that AI models need to be generalizable to a reasonable extent, for example, to function well in different patient populations, locations, and over time. There should be built-in or external quality assessment tools that can monitor model performance with new data inputs or better yet incorporate new data to improve performance. A third domain is transparency and explainability. Transparency means that sufficient information about the design of AI products should be available to allow end users and the public to assess the quality of the AI models. Explainability allows clinicians and patients to understand the factors behind AI models' results and is key to inspire confidence and trust. The last domain is ethics. AI models should be derived from diverse datasets representative of the disease population and scrutinized of underlying biases in data. Explainability can be very helpful to show that the inner workings of AI models do not bias against certain groups of patients. When built and used correctly, AI models could significantly decrease existing bias and inequalities in health care.

CLINICS CARE POINTS

- When evaluating AI/ML algorithms for clinical applications, pay close attention to whether the algorithms have been externally validated, tested in applicable and inclusive patient populations, and have reasonable transparency.

- Partner with ML/AI data scientists and consider participation in clinical trials that evaluate AI/ML products.

DISCLOSURE

M.K. Kanwar serves on the Advisory Board for Abiomed. S. Li, G.W. Hickey, and M.M. Lander have nothing to disclose.

REFERENCES

1. Turing AM. I.—Computing machinery and intelligence. *Mind* 1950;LIX(236):433–60.
2. Bohr A, Memarzadeh K. The rise of artificial intelligence in healthcare applications. In: Bohr A, Memarzadeh K, editors. *Artificial intelligence in healthcare*. Cambridge, MA: Academic Press; 2020. p. 25–60.
3. Ambrosy AP, Fonarow GC, Butler J, et al. The global health and economic burden of hospitalizations for heart failure: lessons learned from hospitalized heart failure registries. *J Am Coll Cardiol* 2014;63:1123–33.
4. Benjamin EJ, Virani SS, Callaway CW, et al. Heart disease and stroke statistics-2018 update: a report from the American Heart Association. *Circulation* 2018;137:e67–492.
5. Ni H, Xu J. Recent trends in heart failure-related mortality: United States, 2000-2014. *NCHS Data Brief* 2015;(231):1–8.
6. Rogers JG, Pagani FD, Tatroles AJ, et al. Intrapericardial left ventricular assist device for advanced heart failure. *N Engl J Med* 2017;376(5):451–60.
7. Slaughter MS, Rogers JG, Milano CA, et al. Advanced heart failure treated with continuous-flow left ventricular assist device. *N Engl J Med* 2009;361:2241–51.
8. Rose EA, Gelijns AC, Moskowitz AJ, et al. Long-term use of a left ventricular assist device for end-stage heart failure. *N Engl J Med* 2001;345:1435–43.
9. Mehra MR, Uriel N, Naka Y, et al. A fully magnetically levitated left ventricular assist device - final report. *N Engl J Med* 2019;380(17):1618–27.
10. Morine KJ, Kiernan MS, Pham DT, et al. Pulmonary artery pulsatility index is associated with right ventricular failure after left ventricular assist device surgery. *J Card Fail* 2016;22:110–6.
11. Matthews JC, Koelling TM, Pagani FD, et al. The right ventricular failure risk score: a pre-operative tool for assessing the risk of right ventricular failure in left ventricular assist device candidates. *J Am Coll Cardiol* 2008;51:2163–72.
12. Kormos RL, Teuteberg JJ, Pagani FD, et al. Right ventricular failure in patients with the HeartMate II continuous-flow left ventricular assist device: incidence,

- risk factors, and effect on outcomes. *J Thorac Cardio-vasc Surg* 2010;139(5):1316–24.
13. Drakos SG, Janicki L, Horne BD, et al. Risk factors predictive of right ventricular failure after left ventricular assist device implantation. *Am J Cardiol* 2010; 105:1030–5.
 14. Johnson KW, Soto JT, Glicksberg BS, et al. Artificial intelligence in cardiology. *J Am Coll Cardiol* 2018; 71(23):2668–79.
 15. Camacho DM, Collins KM, Powers RK, et al. Next-generation machine learning for biological networks. *Cell* 2018;173:1581–92.
 16. Domingos P. A few useful things to know about machine learning. *Commun ACM* 2012;55:78–87.
 17. LeCun Y, Bengio Y, Hinton G. Deep learning. *Nature* 2015;521(7553):436–44.
 18. Esteva A, Chou K, Yeung S, et al. Deep learning-enabled medical computer vision. *NPJ Digit Med* 2021;4:5.
 19. Singh SP, Wang L, Gupta S, et al. 3D deep learning on medical images: a review. *Sensors* 2020;20: 5097.
 20. Christiansen EM, Yang SJ, Ando DM, et al. In silico labeling: predicting fluorescent labels in unlabeled images. *Cell* 2018;173:792–803.e9.
 21. Ting DSW, Pasquale LR, Peng L, et al. Artificial intelligence and deep learning in ophthalmology. *Br J Ophthalmol* 2019;103:167–75.
 22. Chilamkurthy S, Ghosh R, Tanamala S, et al. Deep learning algorithms for detection of critical findings in head CT scans: a retrospective study. *Lancet* 2018;392:2388–96.
 23. Chen PHC, Gadepalli K, MacDonald R, et al. An augmented reality microscope with real-time artificial intelligence integration for cancer diagnosis. *Nat Med* 2019;25:1453–7.
 24. Zhang J, Xie Y, Pang G, et al. Viral pneumonia screening on chest X-Rays using confidence-aware anomaly detection. *IEEE Trans Med Imaging* 2020;40(3):879–90.
 25. Zhang J, Gajjala S, Agrawal P, et al. Fully automated echocardiogram interpretation in clinical practice: feasibility and diagnostic accuracy. *Circulation* 2018;138:1623–35.
 26. Ghorbani A, Ouyang D, Abid A, et al. Deep learning interpretation of echocardiograms. *NPJ Digit Med* 2020;3:1–10.
 27. Apostolopoulos ID, Mpesiana TA. Covid-19: automatic detection from x-ray images utilizing transfer learning with convolutional neural networks. *Phys Eng Sci Med* 2020;43:635–40.
 28. Devlin J, Chang MW, Lee K, et al. Bert: pre-training of deep bidirectional transformers for language understanding. *arXiv*; 2018.
 29. Li F, Jin Y, Liu W, et al. Fine-tuning bidirectional encoder representations from transformers (BERT)-based models on large-scale electronic health record notes: an empirical study. *JMIR Med Inform* 2019;7:e14830.
 30. Choi E, Schuetz A, Stewart WF, et al. Using recurrent neural network models for early detection of heart failure onset. *J Am Med Inform Assoc* 2017;24(2): 361–70.
 31. Adler ED, Voors AA, Klein L, et al. Improving risk prediction in heart failure using machine learning. *Eur J Heart Fail* 2020;22(1):139–47.
 32. Greenberg B, Adler E, Campagnari C, et al. A machine learning risk score predicts mortality across the spectrum of left ventricular ejection fraction. *Eur J Heart Fail* 2021;23(6):995–9.
 33. Jing L, Cerna AEU, Good CW, et al. A machine learning approach to management of heart failure populations. *JACC Heart Fail* 2020;8(7): 578–87.
 34. Yao H, Aaronson KD, Lu L, et al. Using a Fuzzy neural network in clinical decision support for patients with advanced heart failure. *IEEE Int Conf Bioinform Biomed* 2019;00:995–9.
 35. Kwon JM, Kim KH, Jeon KH, et al. Artificial intelligence algorithm for predicting mortality of patients with acute heart failure. *PLoS One* 2019;14(7): e0219302.
 36. Lohmanpour NA, Kormos RL, Kanwar MK, et al. A Bayesian model to predict right ventricular failure following left ventricular assist device therapy. *JACC Heart Fail* 2016;4(9):711–21.
 37. Kanwar MK, Lohmueller LC, Kormos RL, et al. A Bayesian Model to predict survival after left ventricular assist device implantation. *JACC Heart Fail* 2018;6(9):771–9.
 38. Wang Y, Simon MA, Bonde P, et al. Decision tree for adjuvant right ventricular support in patients receiving a left ventricular assist device. *J Heart Lung Transplant* 2012;31(2):140–9.
 39. Movahedi F, Kormos RL, Lohmueller L, et al. Sequential pattern mining of longitudinal adverse events after left ventricular assist device implant. *IEEE J Biomed Health* 2019;24(8):2347–58.
 40. Kilic A, Dochtermann D, Padman R, et al. Using machine learning to improve risk prediction in durable left ventricular assist devices. *PLoS One* 2021; 16(3):e0247866.
 41. Jaeger BC, Cantor RS, Sthanam V, et al. Improving mortality predictions for patients with mechanical circulatory support using follow-up data and machine learning. *Circ Genom Precis Med* 2020;13(2): e002877.
 42. Kilic A, Macickova J, Duan L, et al. Machine learning approaches to analyzing adverse events following durable LVAD implantation. *Ann Thorac Surg* 2021; 112(3):770–7.
 43. Shad R, Quach N, Fong R, et al. Predicting post-operative right ventricular failure using video-based deep learning. *Arxiv*; 2021.

44. Stöcklmayer C, Dorffner G, Schmidt C, et al. An artificial neural network-based noninvasive detector for suction and left atrium pressure in the control of rotary blood pumps: an in vitro study. *Artif Organs* 1995;19(7):719–24.
45. Moscato F, Granegger M, Edelmayer M, et al. Continuous monitoring of cardiac rhythms in left ventricular assist device patients. *Artif Organs* 2014;38(3):191–8.
46. Mason NO, Bishop CJ, Kfoury AG, et al. Noninvasive predictor of HeartMate XVE pump failure by neural network and waveform analysis. *ASAIO J* 2010;56(1):1–5.
47. Hohmann S, Veltmann C, Duncker D, et al. Initial experience with telemonitoring in left ventricular assist device patients. *J Thorac Dis* 2018;1(1):S853–63.
48. Stehlik J, Schmalfuss C, Bozkurt B, et al. Continuous wearable monitoring analytics predict heart failure hospitalization. *Circ Heart Fail* 2020;13(3):e006513.
49. Smedira NG, Blackstone EH, Ehrlinger J, et al. Current risks of HeartMate II pump thrombosis: non-parametric analysis of interagency registry for mechanically assisted circulatory support data. *J Heart Lung Transpl* 2015;34(12):1527–34.
50. Zweck E, Thayer KL, Helgestad OKL, et al. Phenotyping Cardiogenic Shock. *J Am Heart Assoc* 2020;10(14):e020085.
51. Zhang R, Ma S, Shanahan L, et al. Discovering and identifying New York heart association classification from electronic health records. *BMC Med Inform Decis* 2018;18(Suppl 2):48.
52. Li Y, Rao S, Solares JRA, et al. BEHRT: transformer for electronic health records. *Sci Rep* 2020;10(1):7155.
53. Genovese D, Rashedi N, Weinert L, et al. Machine learning-based three-dimensional echocardiographic quantification of right ventricular size and function: validation against cardiac magnetic resonance. *J Am Soc Echocardiogr* 2019;32(8):969–77.
54. Beecy AN, Bratt A, Yum B, et al. Development of novel machine learning model for right ventricular quantification on echocardiography—a multimodality validation study. *Echocardiography* 2020;37(5):688–97.
55. Chen XJ, Collins LM, Patel PA, et al. Heart sound analysis individuals supported with left ventricular assist device: a first look. *Comput Cardiol* 2020;00:1–4.
56. Misumi Y, Miyagawa S, Yoshioka D, et al. Prediction of aortic valve regurgitation after continuous-flow left ventricular assist device implantation using artificial intelligence trained on acoustic spectra. *J Artif Organs* 2021;24(2):164–72.
57. Lüneburg N, Reiss N, Feldmann C, et al. Photographic LVAD driveline wound infection recognition using deep learning. *Stud Health Technol Inform* 2019;260:192–9.
58. Esteva A, Robicquet A, Ramsundar B, et al. A guide to deep learning in healthcare. *Nat Med* 2019;25(1):24–9.
59. Rajkomar A, Oren E, Chen K, et al. Scalable and accurate deep learning with electronic health records. *NPJ Digit Med* 2018;1(1):18.
60. Houser SR. The American Heart Association's New Institute for Precision Cardiovascular Medicine. *Circulation* 2016;134(24):1913–4.
61. Molina EJ, Shah P, Kiernan MS, et al. The Society of Thoracic Surgeons Intermacs 2020 Annual Report. *Ann Thorac Surg* 2021;111:778–92.
62. Desai RJ, Wang SV, Vaduganathan M, et al. Comparison of machine learning methods with traditional models for use of administrative claims with electronic medical records to predict heart failure outcomes. *JAMA Netw Open* 2020;3(1):e1918962.
63. Christodoulou E, Ma J, Collins GS, et al. A systematic review shows no performance benefit of machine learning over logistic regression for clinical prediction models. *J Clin Epidemiol* 2019;110:12–22.
64. Ginestra JC, Giannini HM, Schweickert WD, et al. Clinician perception of a machine learning-based early warning system designed to predict severe sepsis and septic shock. *Crit Care Med* 2019;47(11):1477–84.
65. Lundberg S, Lee SI. A unified approach to interpreting model predictions. *Arxiv*; 2017.
66. Tseng PY, Chen YT, Wang CH, et al. Prediction of the development of acute kidney injury following cardiac surgery by machine learning. *Crit Care* 2020;24(1):478.
67. Bodenheimer T, Sinsky C. From triple to quadruple aim: care of the patient requires care of the provider. *Ann Fam Med* 2014;12(6):573–6.
68. Kelly CJ, Karthikesalingam A, Suleyman M, et al. Key challenges for delivering clinical impact with artificial intelligence. *BMC Med* 2019;17(1):195.